TEST CHANGE

Beckwith-Wiedemann Syndrome (BWS) and Russell-Silver Syndrome (RSS) by Methylation-Specific MLPA

3001635, BWS-RSS DD

Specimen Requirements:	
Patient Preparation:	
Collect:	Lavender (EDTA), pPink (K2EDTA), or yYellow (ACD sSolution A)
Specimen Preparation:	Transport 3 mL whole blood. (Min: 12 mL)
Transport Temperature:	Refrigerated. Also acceptable: Ambient.
Unacceptable Conditions:	
Remarks:	
Stability:	Room temperatureAmbient: 1 week; Refrigerated: 1 month; Frozen: Unacceptable6 months
Methodology:	Multiplex Ligation-Ddependent Probe Amplification (MLPA)
Performed:	Varies
Reported:	12-14 days
Note:	
CPT Codes:	81401
New York DOH Approval Status:	Specimens from New York clients will be sent out to a New York DOH approved laboratory, if possible.

Interpretive Data:

Refer to report. Characteristics of Beckwith-Wiedemann syndrome (BWS) and Russell-Silver syndrome (RSS): BWS is a phenotypically variable overgrowth syndrome associated with an increased risk for embryonal tumor development, neonatal hypoglycemia, macroglossia, macrosomia, hemihyperplasia, omphalocele, renal abnormalities, and ear creases or pits. RSS is characterized by pre- and postnatal growth deficiency, proportionate short stature, developmental delay, learning disabilities, limb-length asymmetry and distinctive faces.
Prevalence: BWS occurs 1 in 10,000-13,700 newborns; RSS 1 in 100,000 newborns.
Inheritance: BWS - 85 percent of cases are sporadic and 15 percent autosomal dominant; RSS - 60 percent of cases are sporadic, 40 percent unknown, rarely autosomal dominant or recessive.
Penetrance: RSS - complete; BWS - incomplete; individuals with a pathogenic CDKN1C variant will be asymptomatic if the variant is on the allele normally silenced due to imprinting.
Cause: BWS - 50 percent by loss of maternal methylation at imprinting center (IC)2, 20 percent by paternal uniparental disomy (UPD) of chromosome 11p15; 5 to 10 percent by pathogenic CDKN1C sequence variants, 5 percent by maternal methylation of IC1, 1 percent by chromosome rearrangements or duplications. RSS - 35 to 50 percent by paternal hypomethylation of IC1, 10

~~percent by maternal UPD of chromosome 7.~~
~~Clinical Sensitivity: 75 percent for BWS; 35-50 percent for RSS.~~
~~Methodology: Methylation-specific multiplex ligation probe amplification (MLPA).~~
~~Analytical Sensitivity and Specificity: 99 percent.~~
~~Limitations: This assay determines methylation patterns of IC1 and IC2 for chromosome 11p15. Disease mechanisms causing BWS and RSS that do not alter methylation patterns, such as sequence variants in *CDKN1C*, maternal UPD of chromosome 7 or chromosomal translocations, and inversions or duplications, will not be assessed. Diagnostic errors can occur due to rare sequence variations.~~

~~This test was developed and its performance characteristics determined by ARUP Laboratories. It has not been cleared or approved by the US Food and Drug Administration. This test was performed in a CLIA certified laboratory and is intended for clinical purposes.~~

~~Counseling and informed consent are recommended for genetic testing. Consent forms are available online.~~

Reference Interval:

By r~~R~~eport